Costello Syndrome
Diagnostic Guidelines

Defining the criteria to diagnose a multiple congenital anomaly syndrome takes many years, many patients and remains largely unscientific, often relying on the “gestalt” (overall impression) of a syndrome to make the final diagnosis.

Costello’s first reports in 1971 and 1977 were expanded by der Kaloustian (1991), and Martin and Jones (1991). Recent review articles characterize over 100 patients (Hennekam, 2003), and summarize neurological and behavioral issues (Kawame et al., 2003; Axelrad et al., 2004, Delrue et al., 2003), cardiac complications (Lin et al., 2002), orthopedic problems (Yassir et al., 2003), malignancies (Gripp et al, 2003), and the adult appearance (White et al., 2005).

A clinical diagnosis of Costello syndrome can now be confirmed by testing for specific mutations in the HRAS gene.

WEB LINKS:
- Online Mendelian Inheritance in Man: http://omim.org/entry/218040
- RASopathiesNet: http://rasopathiesnet.org

For additional information or copies of this brochure contact:
- Costello Syndrome Family Network: http://www.costellosyndromeusa.org/

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This document was developed by Medical Geneticist V.K. Proud and parent, Lisa Schoyer with assistance from Angela Lin, MD and Karen Gripp, MD, Costello Syndrome Professional Advisory Committee members.

In loving memory of V.K. Proud.

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**KEY FEATURES**

The faces of these individuals, who range in age from infancy to adulthood, illustrate the distinctive appearance of Costello syndrome.

**Distinctive facial features**

**Infants (<1 year)**
- Polyhydramnios
- Fetal distress
- C-section (Cesarean section)
- LGA (large for gestational age)
- Feeding problems and hypotonia
- Gastrostomy tube (g-tube) in the first 4 years
- FTT (failure to thrive)
- Growth delay in weight and length but with normal head circumference
- Motor delays

**Toddlers (1-3 years)**
- Distinctive facial features, broad mouth
- Loose, lax skin, soft, deep wrinkles, abnormal creases in palms and soles, stretchy skin, loose joints
- Hernias
- Hypertrophic cardiomyopathy
- Arrhythmia, especially atrial tachycardia
- Strabismus, ptosis
- Malignancy
- DD (developmental delay)

**Children (4-12 years)**
- Short stature
- Distinctive facial features with broad mouth and thick lips
- Kyphoscoliosis, cervical kyphosis
- Remarkably pleasant, sociable, humorous and easy-going personality

**Adolescents/Adults**
- Coarse classic facial features
- Thicker, often curly hair
- Nasal fibromata
- Breast papilloma
- Hyperkeratosis, hyperpigmentation
- Short stature
- Skeletal and orthopedic problems
- DD (developmental disability) / ID (intellectual disability)

**Photo credits** go to the parents of the above children and adults and, for the fourth image on the first panel, Rick Guidotti/Positive Exposure.